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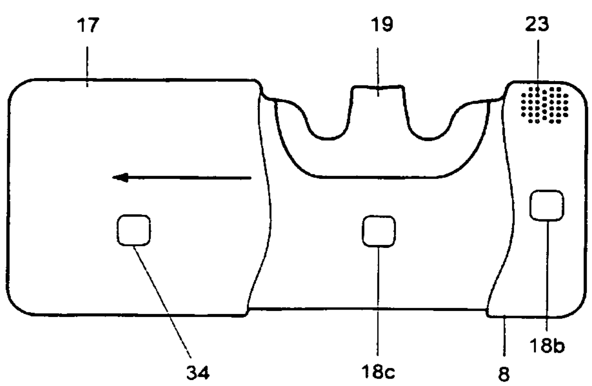
(54) Title: CONTINUOUS DRY POWDER INHALER



(57) Abstract: An continuous dry powder inhaler arrangement is disclosed, the arrangement being provided with pre-metered doses of medication powder onto an exchangeable dose member like a cassette or the like for respiratory administration of medicaments into the deep or upper lung airways. The inhaler presents a device (8) with a case having a sliding lid (17), which can be set in an open position exposing a mouthpiece (19). The arrangement further provides dose counters (18b/18c) and a cassette counter (34). In the state with open lid (17) the device is ready to deliver a prepared pre-metered dose of medication powder upon an inhalation via the exposed mouthpiece (19). Medication drugs are in advance dosed as medication powder and carried by an exchangeable dosing means. The exchangeable dosing member carries a number of sequentially accessible doses, which are sealed to preserve a controlled storing of powder during the total lifetime of the dosing member. Upon an inhalation the cassette carrying a selected dose is released into a longitudinal motion by a forcing spring, whereby the protective foil is cut open to let a nozzle of a suction tube access the powder. By means of a braking arrangement the motion of the cassette is adjusted to such a speed that the time for a continuous delivery of the powder wil be time controlled to an order of 0.5 to 5 seconds. The exchangeable dosing means presents a number of pre-metered doses of deposited dry medication powder.

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Continuous Dry Powder Inhaler

TECHNICAL FIELD

The present invention relates to administration of medication powders into the respiratory tract by releasing powder to be inhaled and more particularly to a dry powder inhaler dispensing a pre-metered dose of medication powder during a controlled inhalation process.

BACKGROUND

The administration of drugs is carried out in a number of different ways in the medical service today. Within health care more and more is focussed on the possibility to dose and distribute powder directly to the lungs of a user by means of an inhaler to obtain effective, quick, and user friendly administration of such substances.

A dry powder inhaler of today, (DPI), represents a device intended for administration of powder into the deep or upper lung airways by oral inhalation. With deep lung should be understood the peripheral lung and alveoli, where direct transport of active substance to the blood can take place. Particle sizes, to reach into the deep lung, should be in a range 0.5 - 3 μm and for a local lung delivery in the range 3 - 5 μm. A larger grain size will easily stick in the mouth and throat, and a smaller grain size may accompany the expiration air out again.

Administration of medication powders into the respiratory tract is a very attractive way for administration of many substances both for local treatments and for systemic treatments. To administer pre-metered doses of drugs by a dry powder inhaler (DPI) through the lung some very important technical basic factors must be met by the system.

A correct dose with a high uniformity of dose is desired from the inhaler. For pre-metered doses of medication substances the relative standard deviation between doses (RSD) should preferably be not more than 5 %.

However, powder having a small grain size will demonstrate a strong tendency to agglomerate, i.e. to clod into larger grains. In the inhalers being used at the moment a large portion of the powder is agglomerated when it is dosed and much powder therefore will stick to the upper respiratory tracts. Technologies for de-agglomeration include advanced mechanical and aerodynamic systems and combinations between electrical and mechanical filling systems that can be seen in for instance U.S. Patent No. 5,775,320, U.S. Patent No. 5,785,049 and U.S. Patent No. 5,740,794.

It is also common to utilize carriers having a larger grain size onto which the fine power is distributed. Upon inspiration the large size grains will stick in the oral cavity while the small grains will be let free and proceed to the lung.

One of the problems upon inhalation of a medication powder is that a relatively large portion of the dose will also stick in the inhaler device. To be able to include all powder and disassemble agglomerates a high air velocity is needed. From a dose given by the inhaler the respiratory dose (grain size less than 5 μm) may often be only 20%.

For achieving a high respiratory dose often a so-called spacer is used to have the small grains evenly distributed in a container from which the inhalation can take place. In principle a dosing device or an inhaler is connected to a container having a relatively large volume and into this container a powder or an aerosol is injected which partly is distributed in the air space and partly sticks to the walls. Upon inhalation from the spacer the fine powder floating free in the air will effectively reach the alveoli. This method in principle has two drawbacks, firstly difficulties to control the amount of medicine emitted to the lung as an uncontrolled amount of powder sticks to the walls of the spacer and secondly difficulties in handling the relatively space demanding apparatus.

Often, devices of prior art technology do not reach a sufficiently high degree of de-agglomeration and an exact dose is not well developed and leaves much to be desired when it comes to dosage conformity and lung deposition effectiveness of the medication substance.

To meet some of these demands an electrostatic dosing of the powder onto a technical means for example a cassette can be performed. An electrostatic dosing onto a device member or cassette was described in our Swedish Patent No. 9802648-7 (SE512 433) and the quality can be improved by utilizing the possibility to classify coarse particles larger than 5 μm to leave those out and dose only fine particles (less than 5 μm) onto the device member or cassette as described in our Swedish Patent No. 9802649-5 (SE512 386).

However, still there is a demand for a device simplifying administration of medication powder by means of an inhaler providing a compact arrangement without the need for instance for a space demanding spacer.

SUMMARY

A continuous dry powder inhaler arrangement is disclosed, the arrangement being provided with pre-metered doses of medication powder deposited onto an exchangeable dose member like a cassette or the like for respiratory administration of medicaments into the deep or upper lung airways. The inhaler presents a compact integrated device with a case having a sliding lid, which can be placed in a closed position covering a mouthpiece or in an open position exposing this exchangeable mouthpiece. In the open lid position the device is ready to deliver a prepared pre-metered dose of medication powder upon an inhalation via the exposed mouthpiece. Medication drugs are in advance dosed as finely divided medication powder and carried by an exchangeable dose member and constitute dry powder substances or dry powder medication formulations prepared for a continuous delivery. The exchangeable dose member, cassette carries a number of sequentially accessible sealed pre-metered doses. The sealing of

the individual doses ensures a sufficiently stable storing of powder during the total lifetime of a dosing cassette. This sealing is cut open during the inhalation process after that the device has been set into the open state by moving the sliding lid to the open position. The mouthpiece and/or the cassette of the device is preferably made out of dissipative and conductive materials to prevent electrostatic charge build-up during inhalation. Upon an inhalation the cassette carrying a selected dose is released into motion by a forcing spring, whereby the protective foil is cut open to let a nozzle of a suction tube access the powder. By a braking arrangement, the motion of the cassette is adjusted to such a speed that the time for the continuous delivery of the powder will be controlled and prolonged to an order of 0.5 to 5 seconds. The exchangeable dose member normally presents a number of electrostatically deposited dry medication powder doses in the form of strips or a series of spots onto the dose member. The DPI is adjusted for a systemic or a local lung setting with respect to activation pressure and optional closing pressure resulting in a 20 to 60 liter/minute inhalation air flow for systemic delivery setting and 40 to 80 liters /minute for a local lung setting. Furthermore the de-agglomeration power is adjusted between 0.1 and 6 watts to be used in the DPI by optimizing the pressure drop and inhalation flow rate by changes to the mouthpiece and/or the dose member and their relation to each other. The DPI activation pressure is further adjusted to a value between 0.5 and 4 kPa and optionally a closing pressure between 0.5 and 4 kPa to eliminate too low power at the start and end of the inhalation. The inhaler arrangement further provides a number of special functions for a safe handling of the device, e.g. control of regular changes of mouthpiece and controls for a utilization of a pre-defined number of cassettes after which it must be discarded.

A continuous dry powder inhaler arrangement according to the present invention is set forth by the independent claim 1 and further embodiments are set forth by the dependent claims 2 to 16.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention, together with further objects and advantages thereof, may best be understood by making reference to the following description taken together with the accompanying drawings, in which:

FIG. 1 illustrates a flow chart of a complete cycle of operating the dry powder inhaler according to the arrangement of the present invention;

FIG. 2 illustrates in an illustrative embodiment a front view of the present inhaler in a closed state;

FIG. 3 illustrates in an illustrative embodiment the left side view of the inhaler in the closed state;

FIG. 4 illustrates in an illustrative embodiment a front view of the inhaler in the open operative state;

FIG. 5 illustrates how the cassette and a box protecting it can be held;

FIG. 6 shows in an illustrative embodiment the cassette in its protective box and illustrates a coding of the box/cassette and a corresponding coding of the cassette opening in the DPI body;

FIG. 7 shows in an illustrative embodiment the mechanism of extracting the cassette from the cassette box and the loading of the cassette into the body of the DPI as the user pushes the cover of the DPI in the closed position;

FIG. 8 shows in an illustrative embodiment the suction tube;

FIG. 9 shows in an illustrative embodiment one of the pre-metered doses onto the cassette and covered by a protective foil, which will be cut open by a cutter tool when the cassette is propelled in direction of the arrows;

FIG. 10 illustrates in an illustrative embodiment the most important internal parts and mechanisms controlling the process of administering a pre-metered dose of powder to a user;

FIG. 11 illustrates one embodiment of the airbrake arrangement for controlling the motion of the cassette during the inhalation process;

FIG. 12 illustrates another embodiment of the airbrake arrangement; and

FIG. 13 illustrates an embodiment of the foil-cutter device.

DESCRIPTION

General definition of the inhaler arrangement

The present invention discloses a dry powder inhalation device (DPI) providing a continuous time controlled delivery of a pre-metered dose during an inhalation of medication powder or powders of the dose. The pre-metered dose is preferably a dose of electro-powder presenting well defined characteristics regarding for instance, particle sizes, electrostatic characteristics, water content and so on. The arrangement comprises in an illustrative embodiment a body, an exchangeable mouthpiece with a suction tube and an exchangeable moving cassette carrying pre-metered sealed doses of dry powder applied in the form of strips or series of spots of powder.

Prefabricated cassettes are individually packed in airtight packages. A cassette box protects the cassette such that when the package is opened and the cassette is removed the user does not come in contact with the sealed

doses. The mechanically coded cassette and cassette box are inserted into an opening into the body of the inhaler arrangement according to the present invention. (see Figures 5 and 6) The cassettes intended for the purpose are correspondingly coded such that only the correct type of cassette fits the opening. Such a coding eliminates the risk that a cassette carrying different powders than the intended can be inserted into the inhaler.

Before the first dose on the cassette can be administered the inhaler must first be opened and closed by pulling the covering lid open and then pushing it shut again. In this way the cassette is extracted from the protective box, schematically illustrated in Figure 7, and brought in the loaded position at the same time as a cassette drive spring is tensioned and secured in this mode by a plunger element.

Removing the cover by pulling it sideways reveals the mouthpiece to which the suction tube is affixed. Thus the cover protects the inhaler and especially the mouthpiece from dirt etc. when the inhaler is not in use. In the process of pulling the cover open the plunger element securing the cassette is pulled out, but the cassette is still kept in the loaded position by another catch mechanism.

The body houses a system for triggering and controlling the administration by means of the inhaler arrangement of pre-metered doses from the cassette, normally a medication drug but other substances are also possible. The system for triggering the delivery of the dose to the user utilizes the inhalation effort to release the catch mechanism that keeps the cassette in its initial spring loaded position as well as opens an inlet for outside air to enter into the interior of the inhaler.

A flap closes the air inlet tightly when the user is not inhaling. The closing force emanates from a spring acting through a system of levers on the catch

mechanism and on the flap. When the user starts to inhale a differential pressure between the surrounding atmosphere and the airways of the user is induced. The induced differential pressure gives rise to an opening force F_p, which counteracts the closing force F_c on the flap. When the differential pressure reaches and supersedes a minimum value the resulting opening force $F_p=F_{minimum}$ overcomes the net closing force F_c of the spring, releasing the catch and opening the flap so that air starts to flow into the inhaler. Referring to Figure 10 it is realized that the minimum required opening force corresponding to a minimum value of differential pressure can easily be adjusted by using a different spring **13** with a different rate, or changing the positions of the pivot points for the levers **28** and **26,** or by using a different lever geometry, or a combination of these methods. In this way the required minimum force $F_p = F_{minimum}$ to open the flap can easily be chosen to suit the particular DPI and serve the objectives of the DPI to the best advantage. The DPI activation pressure is further adjusted to a value between 0.5 and 4 kPa and optionally a closing pressure between 0.5 and 4 kPa to eliminate too low power at the start and end of the inhalation.

A system of levers, which connect the spring with the catch and the flap are preferably designed using suitable low-friction materials and arranged such that the surfaces of the parts, which are in contact in order to transmit power from one to the other or vice versa, are made with rounded shapes and arranged such that the inevitable relative movement is not a rubbing action but a rolling action, such that the point of contact moves like two cogs meshed in a gear wheel to minimize friction in the system. In this way the friction losses and power loss in the mechanical system are minimized, which is important to achieve optimum overall performance for the DPI.

When the catch releases the cassette it is irreversibly propelled forward by the tensed drive spring. An airbrake, which acts on the cassette controls the speed of motion of the cassette such that the time it takes for the cassette to pass by the fixed suction tube of the mouthpiece can be controlled as

desired. The powder of the dose to be administered is in this way carried by the cassette past the fixed nozzle of the suction tube where a passing stream of air rushing into the nozzle of the suction tube sucks up the powder.

It is particularly important that particle size distribution and uniformity of dose is user independent. Each dose on the cassette carrier has an individual airtight seal in the form of a strip of foil or similar, which must be cut open before the dose can be accessed. A sharp cutter in the shape of a wedge with a sharp edge is in a fixed position just before the nozzle such that when the cassette begins to move, the seal of the dose is brought in contact with the cutter before the dose reaches the nozzle. The cutter not only cuts the foil open but it also folds back the foil to make the powder completely accessible for the stream of incoming air resulting from the inhalation.

In different embodiments of the present invention, the drive spring and the airbrake can be given different properties to achieve the desired speed characteristics for the cassette in each embodiment depending on what is the primary purpose of the inhaler in each case. The active dosing time of the DPI during an inhalation can be set for an activation time between 0.5 and 5 seconds. The cassette and airbrake are arranged such that there is a time delay after the catch lets go of the cassette until the first part of the dose reaches the point where the powder of the pre-metered dose will be sucked up by the inhaled air.

The powder is sucked up by the stream of air going into the nozzle at high speed. Further up the suction tube the air speed becomes reduced and the powder is evenly dispersed in the air stream. The suction tube is specially designed using porous walls such that a minimum of powder is retained in the mouthpiece and practically all powder is delivered into the user in continuous manner during a predefined time period. The cassette reaches its

end position in less than 5 seconds after it was released. The user pushes the covering lid to the closed position and leaves the inhaler locked in this way until it is time for a new dose.

A dose indicator in the form of a counter indicates when the last dose of a cassette has been administered and at this point the revolver mechanism stops any further inhalation cycles with the old used up cassette, but releases the cassette from the DPI, so the user can remove the old cassette and replace it with a new one.

Every time a predetermined number of cassettes have been utilized in the inhaler a cassette indicator in the form of a counter indicates that it is time to exchange the mouthpiece. The interval between changes of mouthpiece is short enough to keep a high level of hygiene and to eliminate the risk that retained powder in the suction tube builds up to a point where it risks to become unstuck during an inhalation, giving the user too high a dose. The mouthpiece can easily be removed and replaced with a new one by the user.

When the cassette counter reaches the zero point the DPI is by definition worn out. When all doses of the last cassette have been administered the cassette counter mechanism locks the cassette in the DPI so it cannot be removed from the DPI. The user is left with no option but to discard the whole inhaler including the last cassette and get a new inhaler if further medication is necessary.

<u>Description of a preferred embodiment of the continuous inhaler device</u>

The exterior of the inhaler device is schematically illustrated in Figures 2, 3 and 4. Pulling a cover **17** opens the DPI and gives the user access to the mouthpiece **19**, which is used for inhaling doses of medication powder, one by one through the DPI. Pushing the covering lid back into the initial position closes and locks the arrangement. During storage and

transportation the DPI should be in the closed state such that the cover **17** gives adequate protection of the mouthpiece **19** against ingress of dirt etc. The inhaler body houses a system for triggering and controlling the administration of the doses of dry powder from the dose carrier, referred to as a cassette **4** (Figures 5, 6 and 7), to be handled by the user utilizing the device for inhaling dry powder normally being a medication drug, even if other substances are also possible.

The mouthpiece **19** (Figure 4) comprises a suction tube **33** (Figures 8 and 10) and a mechanism for attaching the exchangeable mouthpiece to the body **8** (Figure 4)of the DPI. Once the user has opened the DPI he or she has easy access to the comfortably formed mouthpiece with the top end of the suction tube arranged to make the inhalation as easy as possible for a user. The DPI is adjusted for a systemic or a local lung setting with respect to activation pressure and optional closing pressure resulting in a 20 to 60 liter/minute inhalation air flow for systemic delivery setting and 40 to 80 liters /minute for a local lung setting. Furthermore the de-agglomeration power is adjusted between 0.1 and 6 watts to be used in the DPI by optimizing the pressure drop and inhalation flow rate by changes to the mouthpiece and/or the device member and their relation to each other. The material of the mouthpiece in contact with the user's mouth is preferably electrically dissipative or conductive so as to equalize any difference in the electric potential between the user and the DPI such that the delivery of the dose is not negatively affected by potential differences. When a predetermined number of cassettes have been administered by the inhaler a built-in cassette counter **18a** (Figure 3) indicates that it is time to exchange the mouthpiece and prompts the user to do this. The interval between changes of mouthpiece is short enough to keep a high level of hygiene and to eliminate the risk that retained powder builds up in the suction tube **33**, which comprises a nozzle **1**, a diffuser **2** and a porous tube **3**. Such a build-up may otherwise come to a point where it risks becoming unstuck during an inhalation, giving the user too high a dose. The mouthpiece can easily be

removed and replaced with a new one by the user. The suction tube is preferably part of the mouthpiece, so that the user exchanges the suction tube in the same operation as the exchange of the mouthpiece without any additional action. Preferably the user is notified by a noise or some other means emitted when the new mouthpiece is properly fitted.

As illustrated in Figure 9 and 10 each dose carrier or cassette **4** carries one or more pre-metered doses of dry powder applied in the form of a strip **5** or a series of spots of powder. Each individual dose **31** has an airtight seal in the form of a strip of foil **24** fixed onto the top of a recess **7** in the cassette where the dose **31** is applied to a dose bed **6**. The cassettes are individually packed in airtight bags (not shown) to stop moisture and other substances from contaminating the cassettes. A cassette box **35** (Figure 6) protects the cassette **4** such that when the bag is opened and the cassette is removed the user does not come in direct contact with the cassette as illustrated in Figure. 5. The mechanically coded **38** cassette and cassette box **35** (Figure 6) are inserted into an opening **32**, in the inhaler body **8** intended for the purpose and correspondingly coded **38** such that only the correct type of cassette box fits the opening. The coding eliminates the risk that a cassette carrying different powders than the intended is inserted in the inhaler.

Figure 1 describes a complete cycle of operating the DPI by illustrating the actions performed by a user and the events, which the actions give rise to in a flow chart. Taking reference in the flow chart the operation of the present invention is illustrated.

Starting point in Figure. 1 is a step **100**, i.e. the user starts with a completely new DPI and a sealed package containing the first cassette, which is to be loaded into the DPI. But first a dummy cassette loaded into the DPI upon delivery must be removed in a step **110**. If the user is unfamiliar with the DPI, the dummy cassette can be used first to practice the art of

inhalation, before loading a real cassette containing the powder doses. If the user decides to practice with the dummy it is necessary to do as many practice runs, as there are doses on the standard cassette before the dummy can be removed from the DPI.

In next step **120**, the user removes the cassette to be used with its protective box from the bag. The cassette with box, illustrated in Figure. 6, is then inserted in the opening **32** of the DPI in step **130**, taking care that the coding of the cassette and box fits the corresponding coding of the opening. The coding is used to make it impossible to insert the wrong type of cassette into the DPI to make administration of the wrong drug impossible.

The DPI, schematically illustrated in Figures 2, 3 and 4, is opened as previously described, in step **140**, and then closed again, in step **150**. This action by the user accomplishes several things at the same time:

i. The cassette is put in position to deliver the first dose

ii. The drive spring is tightened and secured in the tightened state by a plunger element, so that it cannot unleash accidentally and drive the cassette forward

iii. The dose and cassette counters are activated

When the DPI is in the closed state no accidental administration can happen. The relevant internal moving parts of the DPI are statically balanced using counterweights **15** and **29** as necessary, schematically illustrated in Figure 10, making the DPI insensitive to external forces e.g. forces of inertia, gravitation, accidental blows etc. This means that the DPI is not sensitive to orientation for the inhalation, so the user can inhale in any position, with no negative effects on the administration process. Rough handling e.g. dropping the DPI to the floor when it is in the open state will not easily trigger the release of the cassette from its ready-to-go state.

In step **160** the user opens the inhaler to gain access to the mouthpiece in order to inhale a dose. In the process of opening the DPI the plunger element, securing the drive spring and the cassette, is removed but the cassette is still kept in position, ready to deliver a dose, by another catch mechanism.

The act of inhaling through the mouthpiece of the DPI in step **170** initiates the irreversible process of administering a dose to the user. A distinct sound is emitted from the DPI when the inhalation has triggered the administration of the dose. Preferably different series of sounds are also emitted during the dose delivery and likewise a distinct sound is emitted when the delivery has come to an end, thereby notifying that the delivery has begun, when delivery is ongoing and when delivery has been successfully ended.

To start the dose administration process the body **8** of the DPI houses a system for triggering and controlling the administration of the doses from the cassette to the user. Illustrated in Figure 10 the system, for triggering the delivery to the user, utilizes the inhalation effort to release the catch mechanism **12**, which maintains the cassette in its initial spring loaded position, as well as it opens an inlet **23** for outside air to enter into the interior of the inhaler. The air passes an optional filter (not illustrated) at the inlet to stop dirt particles etc. from entering the DPI.

A moving flap **16** shuts the air inlet **23** tight when the user is not inhaling. The closing force emanates from a spring **13** acting through a system of levers **26** and **28** on the flap as well as on the catch mechanism that is keeping the cassette **4** from moving. When the user starts to inhale a differential pressure between the surrounding atmosphere and the airways of the user is induced. The induced differential pressure gives rise to an opening force, which counteracts the closing force onto the flap. When the

differential pressure reaches and supersedes a well-defined minimum value the resulting opening force overcomes the force of the spring, releasing the catch **12**, setting the cassette free and opening the flap so that air starts to flow into the inhaler. The minimum pressure differential required, or activation pressure, lies between 0.5 and 4 kPa, i.e. when the intended DPI is going from a ready state to a stage when the electro-dose is starting to be de-agglomerated inside the mouthpiece **19** and inhaled. This activation pressure is by no means strenuous for a user who is likely to feel that air starts to flow immediately after the inhalation has begun.

The system of levers connecting the spring with the catch and the flap is preferably designed using suitable low-friction materials. To minimize friction in the system, according to the preferred embodiment, it is preferably designed such that the surfaces of the parts **14**, which are in contact with each other in order to transmit power from one to the other or vice versa, are made with rounded shapes and arranged such that the inevitable relative movement between the parts is not a rubbing action but a rolling action making the point of contact move like two cogs meshed in a gear wheel. In this way friction loss and consequently power loss in the mechanical system is minimized, which is important to achieve optimum overall performance of the DPI.

When the catch releases the cassette it is irreversibly propelled forward by the tensed drive spring **9**. An airbrake **22** is exemplified by two embodiments schematically illustrated in Figures 11 and 12. The airbrake acts on the cassette to control the speed of motion of the cassette such that the time it takes for the cassette to pass by the fixed suction tube **33** of the mouthpiece is suitable with respect to the intended release time of powder for the inhalation process. The foil cutter **11** illustrated in Figures. 9 and 10 is used to cut and open up the foil **24** that seals a recess **7** carrying the pre-metered dose **31** on the cassette surface. Thus, the foil **24** protects the dose **31** on the dose bed **6** harboring in the recess. The cutter **11** sits in a fixed position

such that when the cassette is pushed past the cutter it cuts through the protective foil and opens it up just in front of the nozzle **1,** which is the inlet part of the suction tube **33**. The cutter thus makes the dose accessible. As the cassette is pushed towards the nozzle the approaching layer or layers of dose powder particles get sucked up by the passing stream of air just before the inhaled air rushes into the nozzle. The particles are dispersed in the stream of air and continuously delivered to the user.

One of the problems inherent in inhaler devices is that the aerosolized substance tends to stick to the walls of the transport tube, here referred to as the suction tube **33**, which means that valuable substance of the dose may be retained within the suction tube in connection with each inhalation. The risk increases with every inhalation that the user gets an overdose if some of the accumulated retained substance suddenly becomes unstuck and is added to the dose that is being delivered during the inhalation. To eliminate this serious risk the new inhaler device uses an exchangeable mouthpiece **19** with a new design of the part acting as the suction tube **33**, schematically illustrated in Figure 8, comprising three portions; a nozzle **1**, a diffuser **2** and a porous tube **3**. The nozzle, which is very close to the powder source, is directly coupled to the diffuser, which in turn is connected to the porous tube. The stream of air sucked into the nozzle will carry the released powder into the diffuser.

The pressure drop of the DPI is the total pressure drop over the DPI and the major pressure drop within the DPI comes from the de-agglomeration of the electro-dose in a relation $\Delta P_{de\text{-}agglomeration}/\Delta P_{total} \times 100 > 50\ \%$. This can be done by optimizing the aerodynamic design of the mouthpiece and the device member and reducing the overall pressure drop inside the DPI. The mouthpiece should also be aerodynamically optimized to reduce retention of powder and electrically connected by a dissipative material to the user to eliminate electrical fields that will increase the retention in the mouthpiece.

The diffuser **2** is conical in shape and as the diameter of the diffuser increases with the distance from the nozzle the speed of the air decreases. In this way the total pressure loss can be kept to a low value. When the air reaches the porous tube **3** the airspeed is at or near optimum to make the delivery into the user's mouth as effective as possible for a local or system delivery to the deep lung of the precipitated powder particles of a narrow size distribution making up the pre-metered dose.

To obtain a deep lung delivery it is recommended that the inhalation airflow should be between 20 and 40 liters per minute not to have too high flows as the amount of impaction in the upper airways is a function of speed and having a dependency according to the amount of impaction as a function of inhalation airflow and the square of the particle size. An ideal design specification for a deep lung setting of the DPI is a flow 20 to 40 liters per minute and a pressure drop between 1 and 2 kPa not to have too much constraint on the airways making them smaller and by this increasing the velocity of the air in the airways.

The local pressure inside the porous tube is lower than that on the outside, the surrounding atmosphere. The pressure differential will force the air to leak through the wall of the porous tube from the outside to the inside. By careful control of the parameters affecting the leakage, e.g. porosity of the wall, material density, wall thickness etc. an active non-sticking wall is created, which stops the aerosolized powder in the stream of air from sticking to the wall and getting retained within the suction tube. By careful selection of materials and combinations of materials and then applying the mentioned parameters it is possible to control exactly how much and where the air leaks into the parts of the suction tube from the nozzle through the diffuser to the actual porous tube.

The airbrake comprises an enclosed but variable volume of air attached to the moving cassette and arranged such that the volume of air must contract

or expand with the motion of the cassette. One or more vent holes of carefully controlled size let air in or out of the variable volume, thereby controlling the amount of leakage and consequently the effectiveness of the brake. To avoid malfunction of the airbrake through dirt or other matter sticking in the vent holes into the variable volume, the air coming into the DPI may first pass through an optional fine mesh filter (not illustrated). The airbrake can be designed to have a variable leakage through the venting arrangement, thereby varying the braking force to suit the application. The travel time of the cassette can therefore be set between e.g. 0.5 and 5 seconds and the speed characteristics can also be controlled in this manner.

The cassette is arranged so that there is a small time delay after the catch lets go of the cassette until the first part of the dose reaches the point where the powder in the dose is sucked up by the stream of inhaled air. In this short time span the inflow of air is built up and air begins to rush into the suction tube and the cassette accelerates up to speed such that the delivery of powder is at semi-stationary conditions right from the start.

In different embodiments of the present invention, the drive spring and the airbrake can be given different properties to achieve the desired speed characteristics in each embodiment depending on what is the primary purpose of the inhaler in each case. The dose is thus continuously administered for the length of time it takes for the dose, preferably in the form of a strip of powder, to pass by the nozzle. An ideal design specification for the dose delivery is for a deep lung delivery 1.5 seconds starting from the release of the cassette, and for a local lung delivery 0.75 seconds starting approximately 1 second after the release of the cassette, but possible to adjust within the total activation time for the DPI, i.e. from the opening to the closing of the air inlet, if necessary to ensure an optimized result. However, the total inhalation time should not be more than corresponding to 75 % of the user's total inhalation volume. Investigations have shown that for users to have a comfortable inhalation through a DPI the pressure drop

must normally be below 4 kPa and the flow rate between 20 and 80 liters/minute. When the inhalation stops, in step **180**, the cassette is already at rest in its final position.

The user can check the number of remaining doses of the cassette presented at the dose counters **18b** and **18c** (Figure 2), which window is active depends on whether the cassette is in the loaded or the unloaded state. If the inhaled dose was the last one of the cassette, the counter indicates this and it is not possible to perform any more inhalations without first exchanging the present cassette for a new one. If the present cassette is the last one of a set number, different for different DPIs with different types of cassettes, to be accepted by the DPI before scrapping, the cassette counter **18a** indicates this. It is then not possible to remove the last cassette but the inhaler, including the mouthpiece together with the cassette is discarded.

In step **190** the user closes the DPI. If the cassette is used up at this point it must be exchanged for a new one. After a predetermined number of cassettes, the number depending on the type of cassette and the number of doses per cassette, the cassette counter indicates that the mouthpiece is used up and should be exchanged for a new one by the user, which is easy to do. The reasons for exchanging the mouthpiece are as mentioned previously two; to maintain a high standard of hygiene throughout the life of the inhaler and to eliminate the risk that retained powder in the suction tube comes unstuck during an inhalation, giving the user too high a dose.

The present dry powder inhaler, DPI provides a general device for dispensing powder for inhalation, particularly electro-powder in the form of pre-metered electro-doses. As the present DPI is apt to individually be adapted to every specific kind of electro-powder it will then also constitute an inhaler meeting the requirements for an electrostatic dry powder inhaler, also referred to as an EDPI.

It will be obvious to a person skilled in the art that the inhaler device may be modified and changed in many ways without departing from the scope of the present invention, which is defined by the appended claims.

CLAIMS

1. An inhaler device using pre-metered medication powder or powders onto an exchangeable dose member like a cassette or the like for respiratory administration of an inhalation powder into the deep or upper lung airways, **characterized in**

a compact integrated assembly presenting a case having a first and a second state, the first state with a sliding cover (17) in a closed position enclosing an exchangeable mouthpiece (19), and a second state with the sliding cover (17) in an open position exposing the exchangeable mouthpiece (19), the assembly in the second state becoming loaded and ready to deliver a prepared dose of medication powder (31) upon an inhalation;

that a powder dose (31) of the exchangeable dosing member (35) is a dry powder substance or dry powder medication formulation prepared for a controlled dosing sequence, the exchangeable dose member further providing a number of sequentially accessible doses;

that the exchangeable dose member of the device preserves the physical and pharmacological qualities of the sealed doses, the sealing being provided as a foil (24), the foil sealing a dose being cut open when the device, set into the second state by moving the sliding cover (17) to the open position, experiences a user initiating an inhalation by sucking air through the exchangeable mouthpiece (19).

2. The inhaler device according to claim 1, **characterized in** that the exchangeable mouthpiece (19) optimizes the DPI to an optimum pressure between 0.5 and 4 kPa and an airflow between 20 and 80 liters/minute with respect to the medication powder being inhaled.

3. The inhaler device according to claim 1, **characterized in** a braking arrangement controlling the prolonged active dosing time of the DPI during an activation time between 0.5 and 5 seconds and thereby controlling a dose delivery time set within the activation time of the DPI.

4. The inhaler device according to claim 1, **characterized in** a breath actuation valve controlling the DPI activation upon an inhalation operation by means of an activation pressure being adjustable between 0.5 and 4 kPa, thereby cutting off a low pressure flow at the beginning and optionally end of an inhalation.

5. The inhaler device according to claim 1, **characterized in** having dissipative or conductive materials in the mouthpiece (19) and/or in the exchangeable cassette (4) to prevent electrostatic charge build-up during inhalation.

6. The inhaler device according to claim 1, **characterized in** that the exchangeable mouthpiece (19) is integrated with a suction tube (33) comprising a nozzle (1), a diffuser (2) and a porous tube (3) for adjusting speed of air to an optimum to make delivery of powder into a user's mouth effective for a delivery of the precipitated dose of powder particles to the deep lung.

7. The inhaler device according to claim 3, **characterized in** that the nozzle (1) connected to the exchangeable mouthpiece sweeps close over the pre-metered dosed powder (31) on the dosing cassette immediately after the sealing foil has been opened for access.

8. The inhaler device according to claim 1, **characterized in** that the exchangeable dosing member (35) is mechanically coded to only fit into an inhaler intended for a particular medication powder composition to prevent utilization of an incorrect drug.

9. The inhaler device according to claim 1, **characterized in** that the arrangement comprises dose and cassette indicators being activated when a first exchangeable dosing member (35) in form of the user cassette (4) containing pre-metered doses of inhalation powder is inserted into the arrangement.

10. The inhaler device according to claim 9, **characterized in** that the dose indicator, after a release of a last dose from a present dosing cassette (4), orders an exchange of the cassette (4) before a next inhalation of a dose can be initiated, whereby an inserted cassette in use can not be exchanged before the last pre-metered dose has been released.

11. The inhaler device according to claim 9, **characterized in** that the dose indicator, after a preset number of doses inhaled, orders an exchange of the mouthpiece.

12. The inhaler device according to claim 9, **characterized in** that the cassette indicator keeps track of the number of already exchanged cassettes (4) and when the preset number of cassettes has been reached a last cassette will be locked in the inhaler after the last dose has been emitted, marking that the inhaler device now should be discarded for a new one.

13. The inhaler device according to claim 1, **characterized in** that a new unused arrangement is supplied with an inserted dummy cassette, which may be used for user exercises before being exchanged for a real one containing pre-metered prepared doses of powder.

14. The inhaler device according to claim 13, **characterized in** that the dummy dosing cassette if not directly exchanged for a cassette (4) with pre-metered doses, but is utilized for exercises has to perform a number of simulated inhalation operation corresponding to the number of doses contained by the particular type of dosing member (35), to be able to perform an exchange for a real dosing cassette (4) as controlled by the arrangement.

15. The inhaler device according to claim 1, **characterized in** that the exchangeable member (35) presents pre-metered doses of dry medication powder deposited onto the dosing cassette (4).

16. The inhaler device according to claim 1, **characterized in** that a sound is emitted from the DPI when an inhalation has triggered the administration of the dose, a different series of sounds is emitted during the dose delivery and likewise a distinct sound is emitted from the DPI when the delivery has come to an end, thereby notifying the user that a delivery has begun, when a delivery is ongoing and when a delivery has been successfully ended.

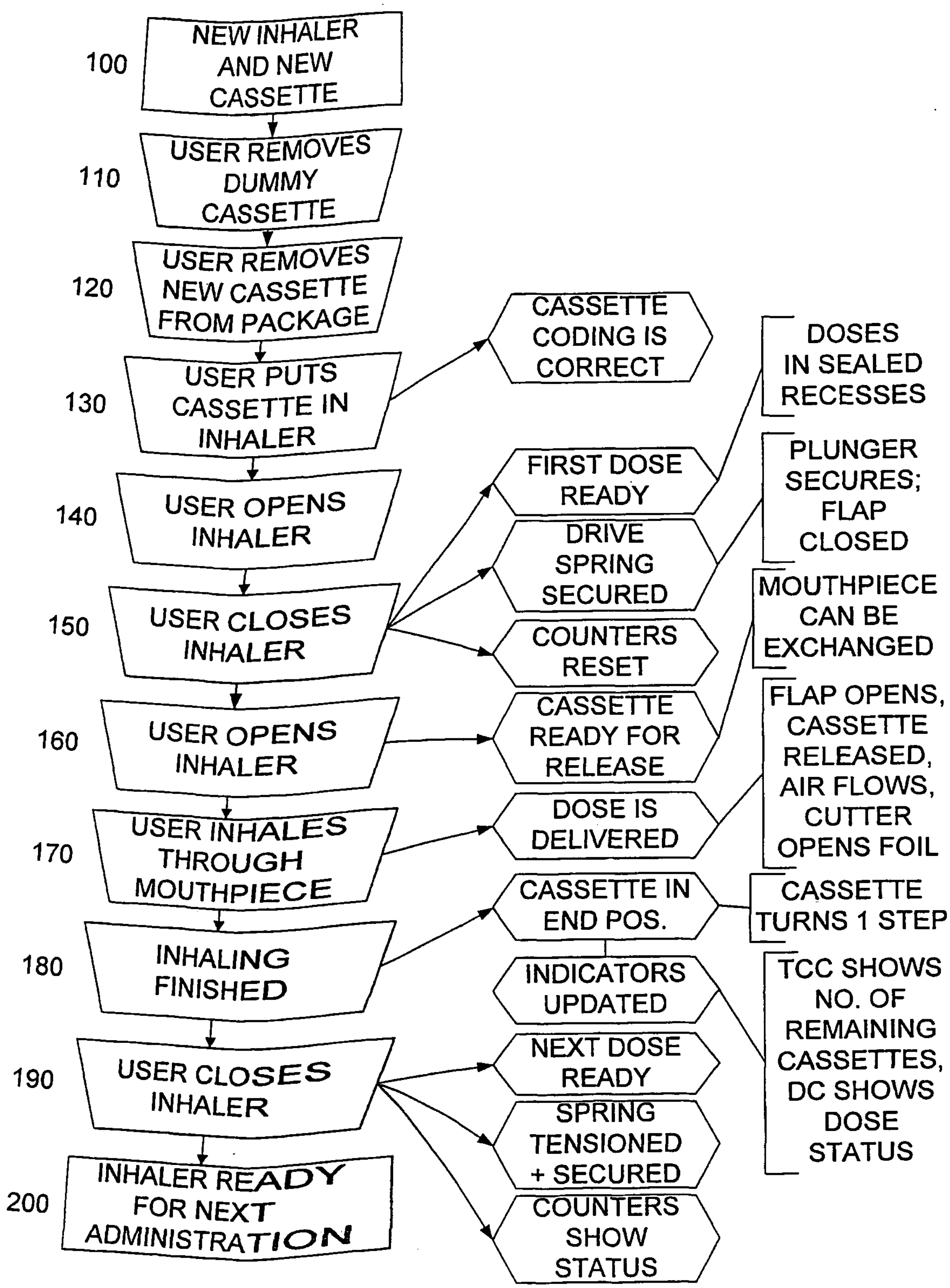
100
NEW INHALER AND NEW CASSETTE
110
USER REMOVES DUMMY CASSETTE
120
USER REMOVES NEW CASSETTE FROM PACKAGE
130
USER PUTS CASSETTE IN INHALER
140
USER OPENS INHALER
150
USER CLOSES INHALER
160
USER OPENS INHALER
170
USER INHALES THROUGH MOUTHPIECE
180
INHALING FINISHED
190
USER CLOSES INHALER
200
INHALER READY FOR NEXT ADMINISTRATION
CASSETTE CODING IS CORRECT
FIRST DOSE READY
DRIVE SPRING SECURED
COUNTERS RESET
CASSETTE READY FOR RELEASE
DOSE IS DELIVERED
CASSETTE IN END POS.
INDICATORS UPDATED
NEXT DOSE READY
SPRING TENSIONED + SECURED
COUNTERS SHOW STATUS
DOSES IN SEALED RECESSES
PLUNGER SECURES; FLAP CLOSED
MOUTHPIECE CAN BE EXCHANGED
FLAP OPENS, CASSETTE RELEASED, AIR FLOWS, CUTTER OPENS FOIL
CASSETTE TURNS 1 STEP
TCC SHOWS NO. OF REMAINING CASSETTES, DC SHOWS DOSE STATUS

Fig. 1

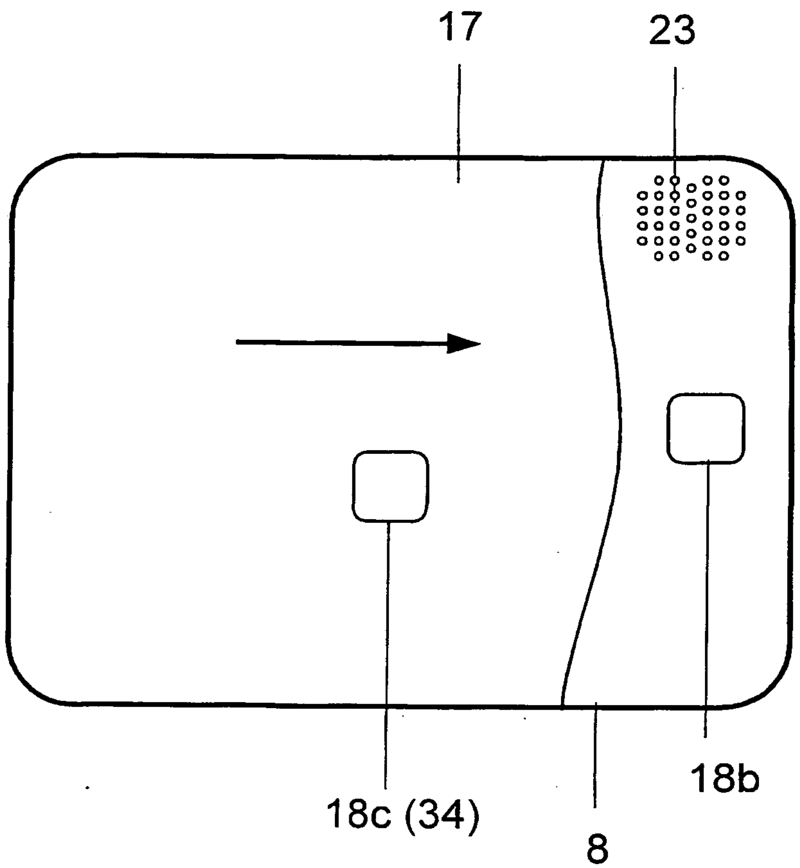

Fig. 2

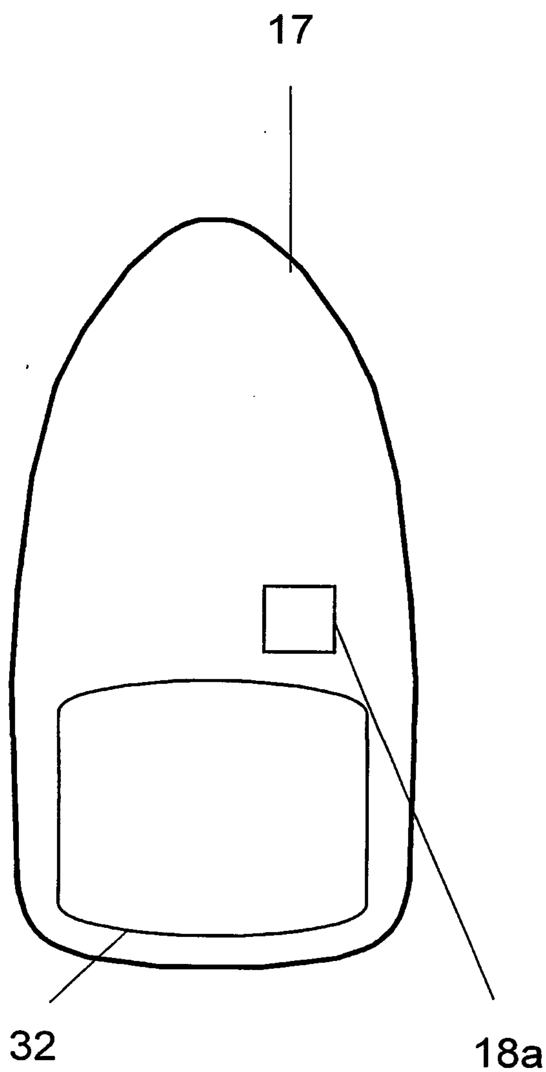

Fig. 3

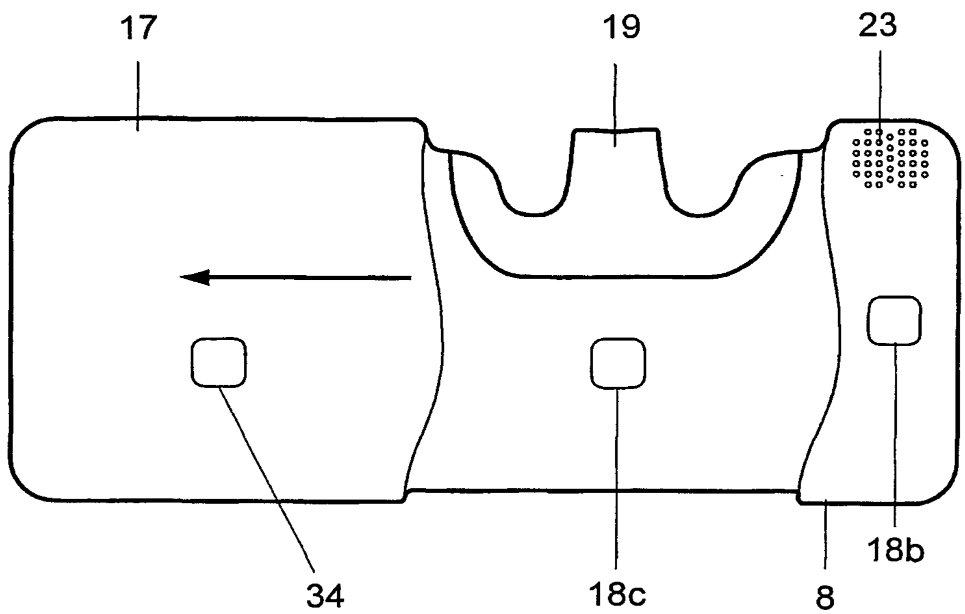

Fig. 4

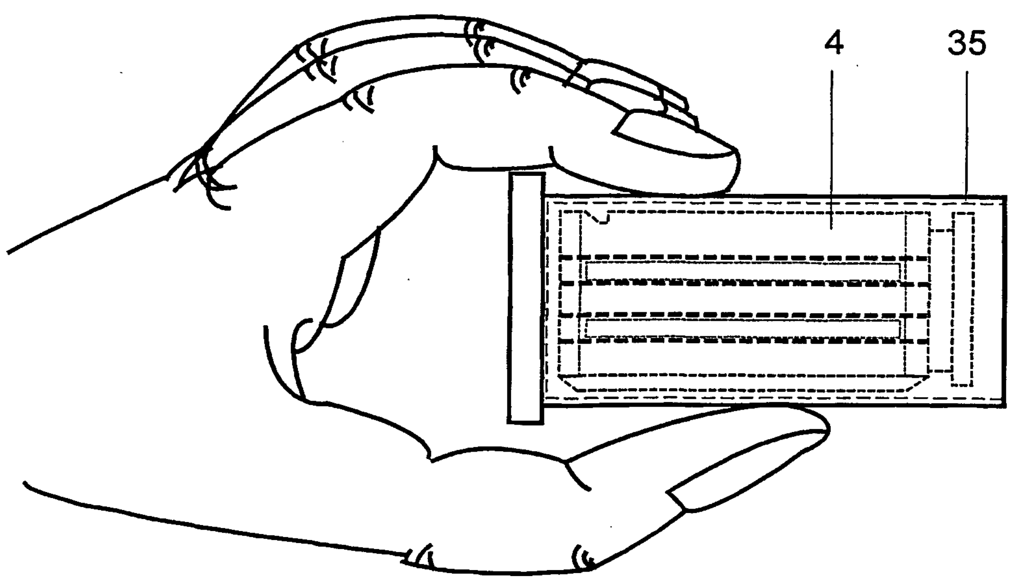

Fig. 5

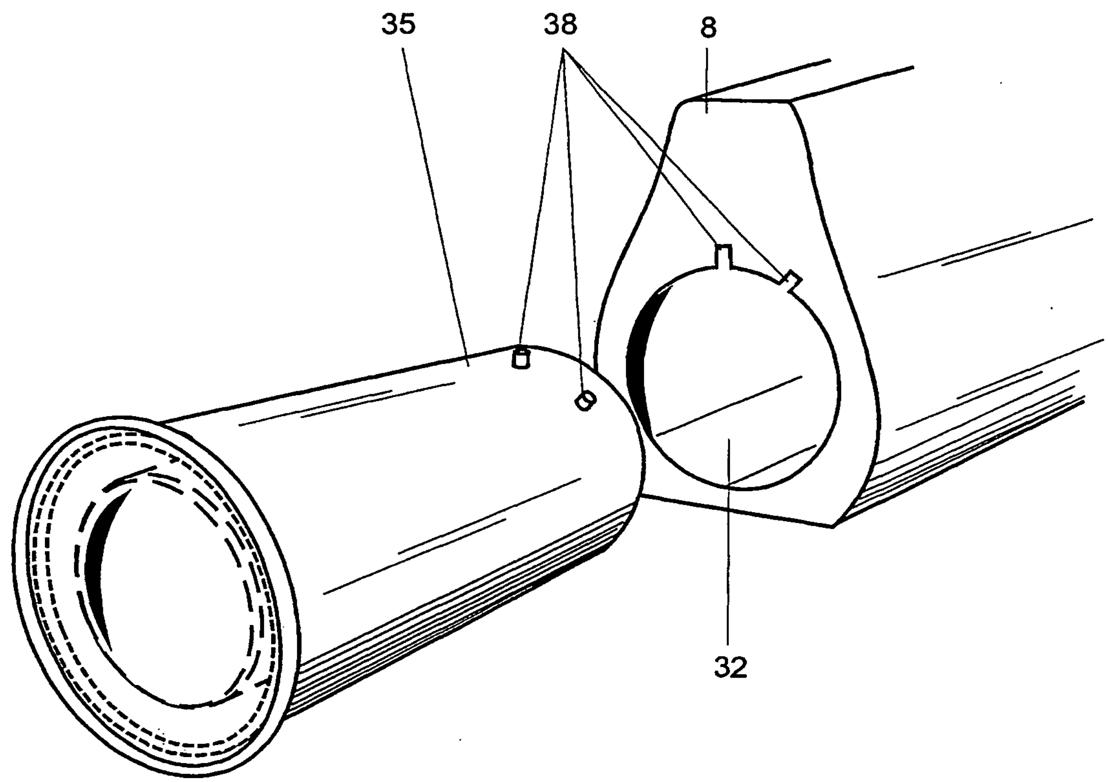

Fig. 6

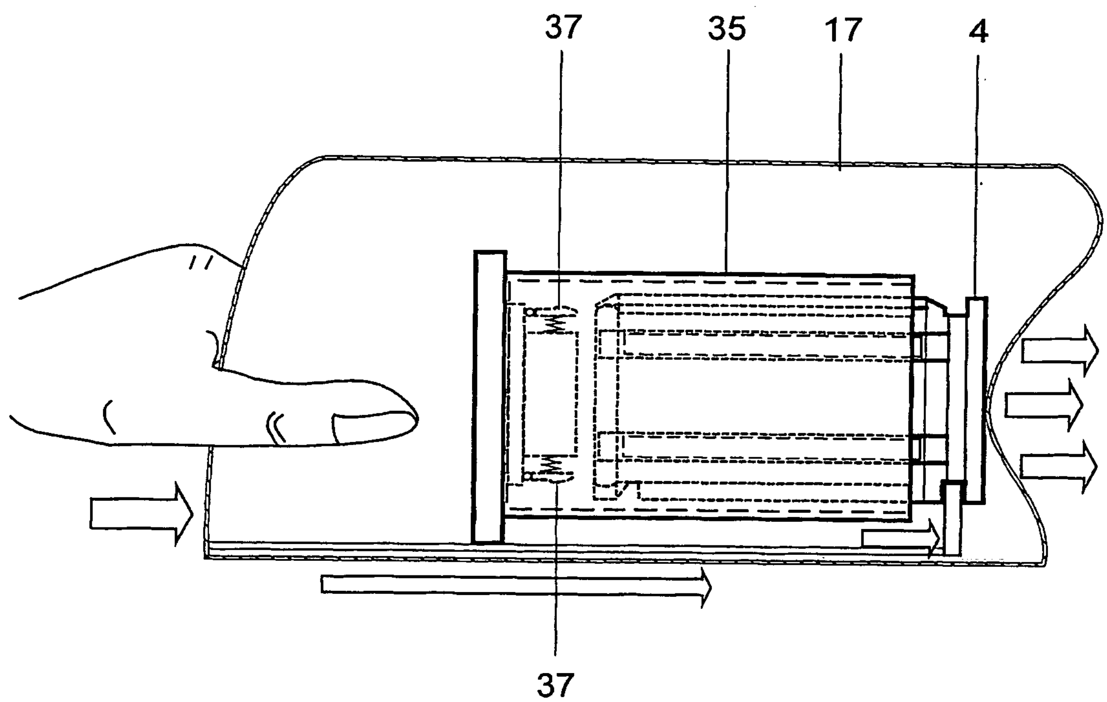

Fig. 7

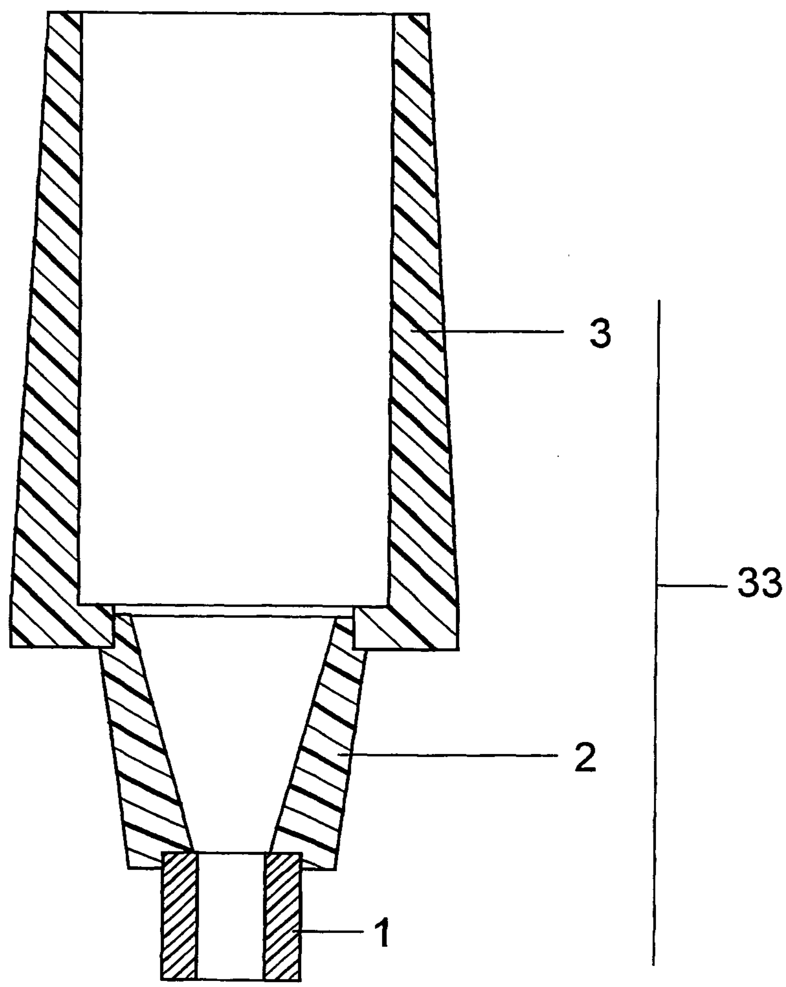

Fig. 8

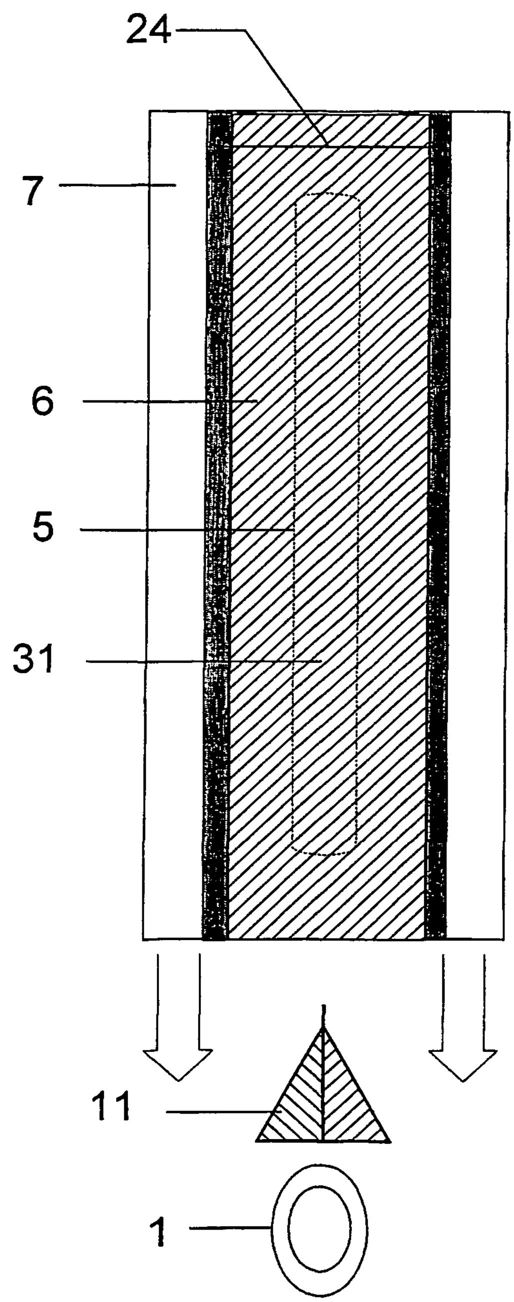

Fig. 9

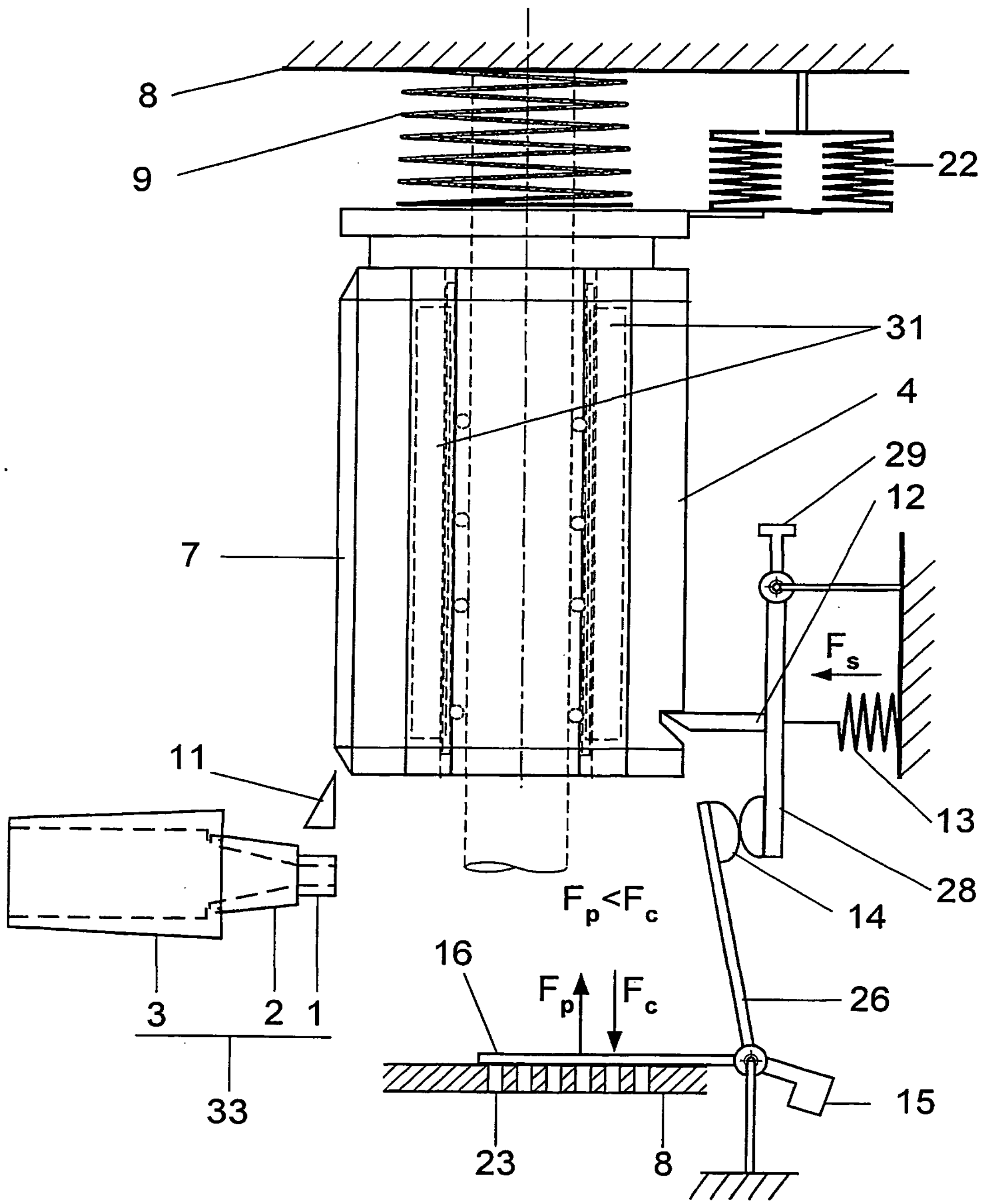

Fig. 10

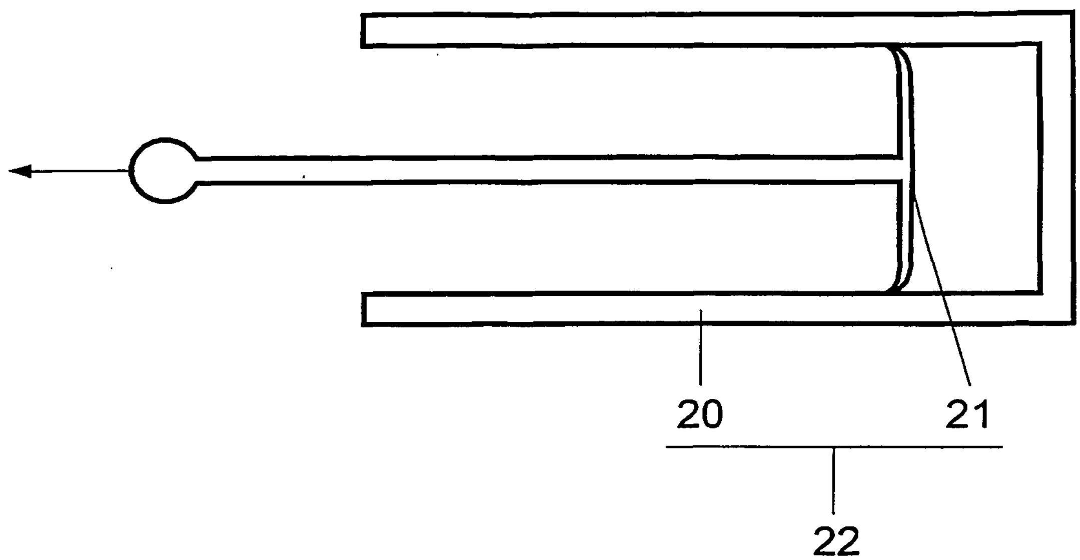

Fig. 11

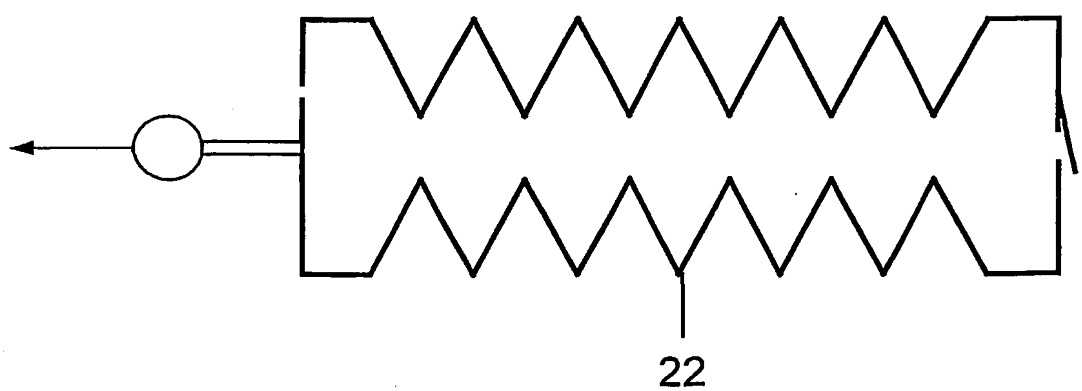

Fig. 12

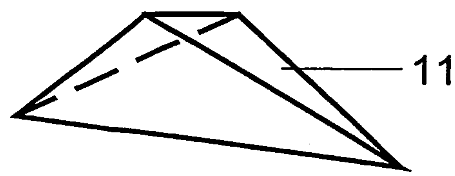

Fig. 13

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 01/02030

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: A61M 15/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6116238 A (THOMAS R JACKSON ET AL), 12 Sept 2000 (12.09.00), abstract, figure --	1-16
A	WO 9013327 A1 (RIKER LABORATORIES, INC), 15 November 1990 (15.11.90), abstract, figure -- --------	1-16

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
22 January 2002	24-01-2002
Name and mailing address of the ISA/ Swedish Patent Office Box 5055, S-102 42 STOCKHOLM Facsimile No. +46 8 666 02 86	Authorized officer Hélène Erikson/EK Telephone No. +46 8 782 25 00